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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,025	12/27/2000	Petrus Johannes Maria Nuijten	99511 US	6121
7590	04/12/2006		EXAMINER	
Bretton L Crockett 230 South 500 East Suite 300 Salt Lake City, UT 84110			FORD, VANESSA L	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 04/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/749,025	NUIJTEN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 15 December 2005.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 7,10,11,19-22,24,28-32,34 and 36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 7,10,11,19-22,24,28-32,34 and 36 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 03 January 2002 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	6) <input type="checkbox"/> Other: _____.

**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 15, 2005 has been entered. Claims 7, 10, 11, 19, 20, 21, 22, 24, 28, 29, 30, 31, 32 and have been amended. Claim 36 has been added. Claims 1-6, 8-9, 12-18, 23, 25-27, 33 and 35 have been cancelled.
  
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

***Rejection Withdrawn***

3. In view of Applicant's amendment and response the rejection under 35 U.S.C. 112, first paragraph, pages 4-12, paragraph 4 of the final Office action is withdrawn.

***Rejection Maintained***

4. The rejection under 35 U.S.C. 112, first paragraph is maintained for claims 22, 24, 28 and 31-32 for the reasons set forth on pages 2-9, paragraph 3 of the Final Office Action.

Art Unit: 1645

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine composition comprising an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium and a pharmaceutical acceptable carrier, wherein the mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin does not reasonably provide enablement for a vaccine composition comprising an immunologically effective amount of any *Salmonella enterica* mutated bacterium, wherein the mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification has not provided enablement for: A) a vaccine comprising any mutated *Salmonella* bacterium from the group consisting of *Salmonella* species *typhimurium*, *enteritidis*, *cholerasuis*, *dublin*, *abortus-ovi*, *abortus-equii*, *derby*, *habar*, *heidelberg*, *agona* and *arizonae* wherein said mutated bacterium lacking flagellin and wherein the vaccine is protective, B) a vaccine comprising any mutated *Salmonella* bacterium from the group consisting of *Salmonella* species *typhimurium*, *enteritidis*, *cholerasuis*, *dublin*, *abortus-ovi*, *abortus-equii*, *derby*, *habar*, *heidelberg*, *agona* and *arizonae*, wherein said mutated bacterium lacking flagellin and wherein the mutated bacterium is attenuated.

The claims are drawn to a vaccine composition. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to *Salmonella* infection or disease induction. The specification teaches that current *Salmonella* vaccines are efficacious however they share a serious disadvantage because they generally induce an antibody population that equals that of an infection with wild-type bacteria because they possess the same antigenic load as the wild-type bacterium. The specification teaches that analysis of antibodies in the serum of *Salmonella*-positive animal does not reveal why the animal is positive, this can be due to vaccination or caused by infection with a virulent strain (page 4). The specification teaches that it would be advantages to have a so-called marker-vaccine comprising an antibody panel that differs from that of the wild-type infection and therefore the host would not make antibodies against the marker (i.e. protein) after vaccination (page 4). The specification teaches that the bacteria is no longer capable of inducing antibodies against at least one antigenic determinant of flagellin or flagella and are considered to be bacteria that do not comprise flagellin or flagella but still possesses all the antigenic determinants (page 6). Example 3 (Experiment 1) of the specification teaches that broilers were inoculated orally, subcutaneously and intramuscularly with a vaccine comprising a wild-type flagellated (fla+) *S. typhimurium* (STMP), a vaccine comprising non-flagellated (fla-) *S. typhimurium* (STM2000) or a vaccine comprising wild-type *S. typhimurium*. The results of this experiment show that 8 out of 10 animals given the wild-type vaccine died and the surviving two had swollen livers with necrotic foci,

Art Unit: 1645

swollen spleen and pericardial edema. One of the STMP inoculated chickens had a slight swollen liver and one of the STM2000 inoculated chickens had a slightly swollen spleen. No further abnormalities were note in the STMP or the STM2000 inoculated groups. Example 3, (Experiment 2) of the specification teaches a vaccine comprising a wild-type flagellated (fla+) *S. typhimurium* (STMP) and a vaccine comprising non-flagellated (fla-) *S. typhimurium* (STM2000) both administered orally into broilers followed by challenge infection with wild-type *S. typhimurium*. The results of the experiment show that a larger proportion of the chickens in the STMP inoculated group was culture positive after direct plating indicates that this strain colonizes the intestinal tract in higher numbers than the STM2000 strain. Example 4 of the specification teaches that pigs were inoculated orally with STMP or STM2000 followed by an oral challenge infection with wild-type *S. typhimurium*. The results of this experiment in Table 5 show that both vaccine strains were able to reduce fecal shedding of the challenge strain significantly.

The teachings of the prior art regarding *Salmonella* nonflagellated mutants are cited below:

Lockman et al (*Infection and Immunity*, January 1990, p. 137-143) teach nonflagelated mutants of *Salmonella typhimurium* (see the Title). Lockman et al teach that flagella enable bacterial cells to move chemotactically in response to stimuli and there is evidence that these organelles function in the attachment of certain bacteria to solid surfaces (page 141, 1<sup>st</sup> column). Lockman et al teach that flagella (H antigen) on the surface of *Salmonella typhimurium* have been characterized as virulence factors that help the bacteria move towards and adhere to the host cells (page 137, 1<sup>st</sup> column). Lockman et al teach that passive immunization of mice with anti-H antiserum did not protect the animals from a lethal challenge with virulent organisms, although the antiserum inhibited bacterial adherence to intestinal epithelium *in vitro* (page 137, 1<sup>st</sup> column). Lockman et al teach that nonflagellated strains colonized the intestinal tracts of orally vaccinated mice as well as isogenic flagellated strains yet did not confer equal protection from subsequent lethal challenge by motile *S. typhimurium* (page 137, 2<sup>nd</sup> column). Lockman et al teach that flagella were necessary for *S. typhimurium* to invade and cause severe disease and the nonflagellated strains were equally proficient at colonization of the murine intestinal tract, but these mutants were deficient in invasion of the reticuloendothelial system (2<sup>nd</sup> column, page 141). Hackett et al (*The Journal of Infectious Diseases*, Vol. 157, January 1988) teach protective and nonprotective strains of *Salmonella*. Hackett et al teach that when mice were fed strains of *Salmonella* a limited infection in the Peyer's patches was established and generated resistance to subsequent challenge with virulent *S. typhimurium* C5 and the these five strains of *Salmonella* are termed "protective" because they did not give rise to bacteremia or colonization in the liver or spleen (1<sup>st</sup> column, page 80). Hackett et al teach that also teach eight strains of *Salmonella* and one strain from *E. coli* expressing O-antigens 1,4, 5 and 12 of *S. typhimurium* administered to mice orally that fail to induce resistance to the virulent *S. typhimurium* C5 challenge, these strains are termed "nonprotective" (page 80 in particular, Table 1). Hackett et al teach that *S. typhimurium* C5 and the five protective strains expressed one to two prominent cell envelope polypeptides of 50-55

Art Unit: 1645

kDa which were not expressed by the nonprotective strains with the exception of *S. derby*. Hackett et al teach that these polypeptides were loosely associated with the cell envelope and there molecular mass values of about 50 to 55 kDa suggesting that they might be composed of flagellin. Hackett et al confirmed that six of the "protective" strains in which polypeptides were detected contained flagellin either (the H-1i antigen or the H-2 1 antigen) (page 80 and figures 1B and C). Hackett et al teach that *S. typhimurium* C5 and all five of protective strains examined expressed high levels of flagella whereas only one of the eight nonprotective did so (page 81). Hackett et al suggests a correlation between the expression of high levels of flagellin by a *Salmonella* strain, its ability to colonize mice when given orally and its ability to protect against subsequent oral *S. typhimurium* C5 challenge (page 81). Hackett et al determined that there is a correlation between protection and colonization by administering orally to mice flagella-positive (fla+) and flagella-negative (fla-) strains of *Salmonella*. Hackett et al teach that the fla- colonized the Peyer's patch as well as the fla+ strains and when give orally no strain colonized the spleens of infected mice (1<sup>st</sup> column, page 82). Hackett et al teach that there is a correlation between flagella expression and protective efficacy because mice immunized with fla+ strains showed lower numbers of challenge bacteria in the spleen than did mice immunized with the fla- strains, a result agreeing with the greater protective effects of immunization with the fla+ strains. Hackett et al teach that the levels of challenge strain in the spleens of the immunized mice were similar to three days postinfection, but mice immunized with fla+ strains eliminated the challenge whereas the mice immunized with fla- strains did not (pages 81-82). Hackett et al teach that it is uncertain whether the relative inefficacy of the fla- vaccines results from their inability to elicit immunity to flagella or from their inability (compared with fla+ strains) to induce immune responses to a wider range of bacterial antigens (2<sup>nd</sup> column, page 83). Hackett et al teach that flagella promote the intracellular survival of *Salmonella* after ingestion by macrophages and therefore fla+ and fla- bacteria are perhaps "processed" differently by these cells because macrophages can function as antigen presenting cells and this might lead to qualitative and quantitative differences in immune response (2<sup>nd</sup> column, page 83). Wahdan et al (*Bull World Health Organization*, vol. 52, 1975) teach a nonmotile mutant of *Salmonella typhi* Ty2 which produces high levels of Vi and O titers but is devoid of the flagellar antigen (does not induce formation of H antibody) (page 69). Wahdan et al teach that the TNM1 vaccine was produced with strain TNM1 (page 69). Wahdan et al teach that the TNM1 vaccine is identical to other *S. typhi* whole cell vaccines prepared with Ty2 except that it is devoid of the H antigen and therefore does not interfere with the Widal test for H antibody (page 71). Wahdan et al teach that the TNM1 vaccine did not provide protection. Wahdan et al teach that there is a correlation between the H antibody and protection and suggests that it seems more probable that a property other than the synthesis of flagellar antigen determines immunogenicity and it is absent from the TNM1 non-motile mutant (pages 71-72).

The vaccine composition "is in live attenuated form". The specification teaches that the claimed vaccine compositions can be in a live attenuated form or inactivated (page 11). The specification teaches that the development of live attenuated vaccines

Art Unit: 1645

in general is difficult and time consuming. The specification teaches that fine-tuning of the degree of attenuation is complex because high virulence causes disease and low virulence induces insufficient protection (page 11). The specification teaches that removal of the flagellin gene does not significantly change the level of attenuation (page 11). Lockman et al (*Infection and Immunity*, January 1990, p. 137-143) teach that the role of the flaF25 mutation in the attenuation of *S. typhimurium* is unclear. The flaF25 mutation was correlated with flagellar biosynthesis and was originally described as a deletion of unknown size within the flaF gene cluster but was subsequently report as a deletion of genes flaF1 through flaFV. The flaF25 mutation had been reported to involve not only some of the genes encoding the biosynthesis of flagella but extended into to a previously undescribed virulence gene(s)(2<sup>nd</sup> column, page 137).

The prior art has taught that flagella (H antigen) enable bacterial cells to move chemotactically in response to stimuli and there is evidence that these organelles function in the attachment of certain bacteria to solid surfaces. The prior art has taught flagella have been characterized as virulence factors. The prior art has taught that fla+ strains express one to two proteins of about 50 to 55 kDa which correspond to the H-1i antigen and the H-2 1 antigen (i.e. flagellin) with the exception of *S. derby*. There is a correlation between high level of flagella, colonization and protection regarding protective *Salmonella* strains. The prior art teaches that although fla+ and fla- strains equally colonize the Payers patch, the fla+ strains eliminated challenge bacteria whereas the fla- strains did not. The prior art teaches that live oral *Salmonella* vaccines comprising fla+ strains have been found to be superior against *S. typhimurium* C5 infection in mice. The prior art teaches that fla+ strains may be superior vaccines because macrophages may process bacteria cells that contain flagella differently than those that do not since the prior art has taught that macrophages can function as antigen presenting cells. The prior art has taught that there is a correlation between protection and the H antigen since a nonmotile mutant (lacking the H antigen) of Salmonella typhi did not protect patients against typhoid fever. The prior also teaches that a property other than the synthesis of flagellar antigen determines immunogenicity and it is absent from the TNM1 non-motile mutant. The prior art that the role of attenuation to produce Salmonella nonflagelated mutants is unclear.

Factors to be considered in determining whether undue experimentation is required are set forth in *In re Wands* 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

In view of the teachings of the specification (or the lack thereof) and the teachings of the prior art there is lack of enablement for the a vaccine comprising any mutated *Salmonella* bacterium from the group consisting of *Salmonella* species *typhimurium*, *enteritidis*, *cholerasuis*, *dublin*, *abortus-ovi*, *abortus-equii*, *derby*, *habar*, *heidelberg*, *agona*, *arizona*, *typhi* or *paratyphi A and B*, wherein said mutated bacterium lacking flagellin and the said vaccine composition is protective. The specification has shown that the vaccines comprising mutated bacterium lacking

flagellin from *S. typhimurium* STMP are protective. It is determined that there are limited working examples commensurate in scope with the instant claims and there is limited guidance provided in the specification as to how to make and use vaccine compositions that comprise a mutated from any *Salmonella* bacterium (other than STM2000) lacking flagellin that are protective against Salmonellosis. The skilled artisan is forced into undue experimentation to practice (make and use) the invention as is broadly claimed because the prior art has taught that many strains of fla- are not protective, do not confer protection from subsequent challenge by motile *Salmonella* bacteria and that mutations such as the flaF25 mutation in the attenuation of *Salmonella* bacterium is unclear.

Applicant's Arguments

A) Applicant urges that the cited references fail to challenge the enablement of the invention. Applicant urges that Lockman et al actually teach that while flagella and motility play a part in the ability of *Salmonella typhimurium* to infect tissue culture monolayers *in vitro* flagella are not a virulence factor of *in vivo* murine typhoid. Applicant urges that Lockman et al suggest that the presence or absence of flagella is irrelevant as a virulence factor for *Salmonella*.

B) Applicant urges that Hackett et al show a correlation between mice immunized with fla+ *Salmonella* strains and protection from subsequent infection. Applicant urges that Hackett et al teach that multiple fla+ strains do not confer protection against *S. typhimurium* M206 and *S. derby*. Applicant urges that fla- strains of Hackett et al conferred protection against motile *Salmonella*.

C) Applicant urges that Wahdan et al acknowledged that a property other than the synthesis of the flagellar antigen determines immunogenicity and is absent from this non-motile mutant.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed December 14, 2005 have been fully considered but they are not persuasive.

A) To address Applicant's comment's regarding Lockman et al, it should be noted that flagella played a role in the ability of *Salmonella typhimurium* to invade tissue. Thus, this reference is presented to show that *Salmonella* fla+(with flagella) bacteria are more likely to invade the host (e.g. reach the site of infection) than *Salmonella* fla- (non-motile or mutants wherein the mutated bacteria are not capable of inducing an immune response to at least one antigenic determinant of flagellin).

B) To address Applicant's comments regarding Hackett et al, this reference teaches that there is a correlation between flagella expression and protective efficacy in mice immunized with fla+ and fla- strains. Hackett et al demonstrates that fla+ strains of *Salmonella* eliminated *Salmonella typhimurium* C5 challenge while fla- strains of Salmonella did not. It should be remembered that Hackett et al teach a *S. typhimurium* M206 bacterium that did not synthesize flagella (i.e. mutated bacterium wherein the mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin)(page 81) and is not protective against *Salmonella typhimurium* C5 challenge in mice (page 80, table 1). The claims nor the instant specification define the actual mutation/mutations that are made in the *Salmonella* bacterium. One of skill in the art would not conclude that all strains of *Salmonella enterica* encompassed by the claimed invention are protective based on the teachings

of the prior art. To address Applicant's comments regarding multiple fla+ species that did not confer protection, it should be remembered that the claims are directed to *Salmonella* mutants that are mutated bacteria and are not capable of inducing an immune response to at least one antigenic determinant of flagellin and not fla+ *Salmonella* organisms and not *Salmonella* mutants that have a functional flagella.

C) Although Wahdan et al suggest that other a property other than the synthesis of the flagellar antigen determines immunogenicity and is absent from this non-motile mutant, the prior art reference also teaches that there is a correlation between protection and the H antigen. It should be noted that the nonmotile mutant (lacking the H antigen) of *Salmonella typhi* did not protect patients against typhoid fever.

Thus, the instant specification does not enable all mutated *Salmonella enterica* bacterium encompassed by the claimed invention. The specification is only enabled for vaccine compositions comprising an immunologically effective amount of a *Salmonella typhimurium STMP mutated bacterium* and a pharmaceutical acceptable carrier. In view of all of the above, this rejection under 35 U.S.C. 112, first paragraph is maintained.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 7, 11, 22, 29, 30, 31 and 32 rejected under 35 U.S.C. 102(b) as anticipated by Joys et al (*Journal of General Microbiology*. 1965, 41, 47-55).

Claims 7, 11, 22, 29, 30, 31 and 32 are drawn to an immunologic composition comprising for marking an exposure of a subject to wild-type *Salmonella*, said immunogenic composition comprising an immunologically effective amount of a live mutated bacterium and a pharmaceutically acceptable carrier, wherein said live mutated bacterium is *Salmonella enterica* that in its wild-type form carries flagella and wherein said live mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin in the subject to which it is administered.

Joys et al teach compositions comprising fla- (non-flagellate) *Salmonella typhimurium* bacterium in broth culture (page 48-49). Broth culture is a pharmaceutically acceptable carrier because the instant specification teaches that “such a carrier may be as simple as water, but e.g. also comprise culture fluid in which the bacteria were cultured (page 12). Claim limitations such as “an improved *Salmonella* vaccine” and “an improvement in a marker vaccine” are being viewed as limitations of

intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The claimed limitation "wherein the marker vaccine is in a freeze-dried or sprayed -dried form is being viewed as a process limitation. Joys et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

6. Claims 7, 11, 20, 22, 28, 29, 30, 31 and 32 rejected under 35 U.S.C. 102(b) as anticipated by Lockman et al (*Infection and Immunity*, January 1990, p. 137-143).

Claims 7, 11, 20, 22, 28, 29, 30, 31 and 32 are drawn to an immunologic composition comprising for marking an exposure of a subject to wild-type *Salmonella*, said immunogenic composition comprising an immunologically effective amount of a live mutated bacterium and a pharmaceutically acceptable carrier, wherein said live mutated bacterium is *Salmonella enterica* that in its wild-type form carries flagella and

wherein said live mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin in the subject to which it is administered.

Lockman et al teach compositions comprising fla- (non-flagellate, lacks at least one antigenic determinant of flagellin) *Salmonella typhimurium* bacterium in broth culture containing glucose (page 139). Broth culture is a pharmaceutically acceptable carrier because the instant specification teaches that "such a carrier may be as simple as water, but e.g. also comprise culture fluid in which the bacteria were cultured (instant specification, page 12). Claim limitations such as "an improved *Salmonella* vaccine" and "an improvement in a marker vaccine" are being viewed as limitations of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The claimed limitation "wherein the marker vaccine is in a freeze-dried or sprayed – dried form is being viewed as a process limitation. Lockman et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See

In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 19, 22, 24, 28, 29, 30, 32 and 34 rejected under 35 U.S.C. 102(b) as anticipated by Wahdan et al (*Bull World Health Organ*, Vol. 52, 1975).

Claims 19, 22, 24, 28, 29, 30, 32 and 34 are drawn to an immunologic composition comprising for marking an exposure of a subject to wild-type *Salmonella*, said immunogenic composition comprising an immunologically effective amount of a inactivated mutated bacterium and a pharmaceutically acceptable carrier, wherein said live mutated bacterium is *Salmonella enterica* that in its wild-type form carries flagella and wherein said live mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin in the subject to which it is administered and a marker vaccine.

Wahdan et al teach a vaccine comprising a nonmotile of *Salmonella typhi* Ty2 (TNM1)(see the Abstract and the Title). Wahdan et al teach that the TNM1 was acetone-killed and lyophilized (page 69). Wahdan et al teach that the TNM1 vaccine is identical to other *S. typhi* whole cell vaccines prepared with Ty2 except that it is devoid of the H antigen (lacks at least one antigenic determinant of flagellin) (page 71). Claim limitations such as "an improved *Salmonella* vaccine" and "an improvement in a marker vaccine" are being viewed as limitations of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably

distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Wahdan et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 19, 22, 24, 28, 29, 30, 32 and 34 are rejected under 35 U.S.C. 102(b) as anticipated by Anderson (*GB Patent No. 1,109,179, published April 10, 1968, The London Patent Office*).

Claims 19, 22, 24, 28, 29, 30, 32 and 34 are drawn to an immunologic composition comprising for marking an exposure of a subject to wild-type *Salmonella*, said immunogenic composition comprising an immunologically effective amount of a inactivated mutated bacterium and a pharmaceutically acceptable carrier, wherein said live mutated bacterium is *Salmonella enterica* that in its wild-type form carries flagella and wherein said live mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin in the subject to which it is administered and a marker vaccine.

Anderson teaches stable non-motile strains of *Salmonella typhi* and *Salmonella paratyphi* (A and B) which are devoid of flagella (lacks at least one antigenic determinant of flagellin) capable of producing the TH, AH or BH antibodies (page 1). Anderson teaches that the *Salmonella* organisms used in the vaccine compositions are heat-killed, alcohol-killed or acetone-killed (page 2). Anderson teaches that the vaccine compositions of the invention can be freeze-dried cultures (page 2). Claim limitations such as "an improved *Salmonella* vaccine" and "an improvement in a marker vaccine" are being viewed as limitations of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Anderson anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

***Status of Claims***

9. No claims are allowed.

***Conclusion***

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 28, 2006

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